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Effects of Prolonged Sitting and Walking for Two Days on Postprandial Triglycerides in Men: Interaction with Energy Intake

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Effects of Prolonged Sitting and Walking for Two Days on Postprandial Triglycerides in Men: Interaction with Energy Intake

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Report

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Abstract

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Postprandial hypertriglyceridemia (PPHT), an independent risk factor for atherosclerosis (Smyth and Heron 2006; Nordestgaard, Benn et al. 2007), is strongly associated with metabolic syndrome and cardiovascular diseases (CVD) (Kolovou, Anagnostopoulou et al. 2005). It has been proposed that elevated triglycerides after a high-fat meal may be a postprandial phenomenon (Zilversmit 1979). PPHT are commonly concurrent with sedentary behaviors, such as extended sitting, which amplify PPHT (Levine, Vander Weg et al. 2006). The purpose of this study was to examine the effects of prolonged sitting with or without a balanced caloric diet and walking with a balanced diet on postprandial triglycerides (PPTG). Seven healthy, young men (age, 25.6 ± 3.7 y; height, 174 ± 5 cm; weight, 71.4 ± 6.2kg; VO2max, 49.3 ± 7.7 ml/kg/min) were recruited from a college and from within the Austin community. After 2 days of food and activity control (D1and D2), subjects performed one of three trials in a randomized, cross-over design for 2 days (D3

and D4); (1) active walking with a balanced diet (WB), (2) prolonged sitting with a hyper-caloric diet (SH), and (3) prolonged sitting with a balanced diet (SB). High fat tolerance tests (HFTT) were conducted on the following day, (D5), after 13 hour over-night fasting. Blood samples were obtained in the fasting state and every hour for 6 hours after subjects had eaten a high fat test meal consisting of 1.2 g fat, 1.1 g CHO, 0.2 g protein/kg body mass. All food was provided during the 5-day duration of the study. Body postures, heart rate, and daily steps were monitored. In both sit trials (SH and SB), subjects sat ~320 minutes longer and took 10 times fewer steps than WB. In WB, the total area under the curves for plasma triglycerides (AUC_T TG) was lower, compared to SH by 21.3% ($p<0.001$) and to SB by 19.7% (N.S.; $p = 0.055$), respectively. In WB, the incremental AUC TG (AUC_I TG), an index of postprandial response, was lower than both SH by 17.4% ($p <0.005$) and SB by 20.1% ($p <0.05$), respectively. Postprandial plasma insulin concentration was lower in WB, compared to SH by 19.4% ($p <0.005$) in AUC_T and 18.8 % ($p < 0.05$) in AUC_I. No differences were shown in the metabolic responses between SB and SH despite the diet modifications. These findings indicate that two days of prolonged sitting significantly amplifies PPTG and suppresses insulin action.

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Chapter 1

INTRODUCTION

In modern societies, humans have become progressively inactive and more exposed to high-fat food, increasing the incidence and the risk of obesity and type 2 diabetes (Chakravarthy and Booth 2004). Moreover, during most waking periods, people remain in non-fasting states, barely staying away from eating for 6-8 hours. Inactive behaviors are commonly concurrent with non-fasting states; the combination of the two may significantly enlarge the magnitude of plasma triglycerides. Elevation of plasma triglycerides in the postprandial state is well associated with the incidence of cardiovascular events, atherosclerosis and metabolic syndrome(Nordestgaard, Benn et al. 2007). In addition, recent epidemiologic studies have shown a positive relationship between the time expended on sedentary behaviors and the risk for type 2 diabetes mellitus (Hu 2003). However, it is well known that a single bout of moderate exercise can significantly reduce PPTG for both untrained and trained individuals (Miyashita, Burns et al. 2006; Harrison, O'Gorman et al. 2009), although the attenuating effect is transient (~ 60 hours). It has been also shown that increased daily walking has been associated with enhancement in health and insulin sensitivity (Stephens, Granados et al.; Swartz, Strath et al. 2003), and that brisk walking is effective in attenuating PPTG(Miyashita, Burns et al. 2008). Moreover, a growing number of studies have

emphasized the beneficial effects of walking and standing to mitigate the detrimental effects provoked by a sedentary life style and high-fat diet (Levine, Vander Weg et al. 2006; Zderic and Hamilton 2006). However, previous studies have yielded mixed results on the efficacy of walking in attenuating PPTG (Tsetsonis and Hardman 1996; Katsanos and Moffatt 2004). It is generally assumed that non-exercise activities might not be controlled during periods of prolonged sitting, which is considered a sedentary behavior. Daily variation in non-exercise activity can alter as much as 2,000 kcal/day, implying that the control of daily activity can play an important role in determining the effect of true daily walking (Levine 2007). Unpublished data in our laboratory verified that both moderate exercise and low intensity walking with the careful control of daily activity considerably decreased PPTG (40% and 27%, respectively), compared to the true sitting control. However, it is unclear whether the effect on PPTG resulted from the energy deficit brought on by the caloric expenditure of the exercise or exercise itself. The aim of the present study is to examine whether prolonged sitting with a balanced caloric intake elevates PPTG, compared to increased walking with balanced energy intake. This study also investigates prolonged sitting with a hyper caloric intake, compared to prolonged sitting with a balanced caloric intake.

Chapter 2

REVIEW OF LITERATURE

INTRODUCTION

In this review of the literature, pathogenic pathway, insulin action, aerobic exercise and daily activity on PPTG are discussed. The present paper focuses on activity control and metabolic variables associated with PPTG during active walking or prolonged sitting. Daily ambulatory activities for 2 days and metabolic responses on HFTT will be emphasized.

PATHOGENIC PATHWAY AND POSTPRANDIAL TRIGLYCERIDES

Postprandial hypertriglyceridemia is an abnormal elevation in circulating plasma triglycerides following a high-fat meal, which is an independent risk factor for atherosclerosis (Nordestgaard, Benn et al. 2007) and an indicator of the risk of cardiovascular disease (CVD) (Boquist, Ruotolo et al. 1999). Elevated plasma triglycerides in the postprandial state mostly result from small intestine-induced chylomicron triglycerides (CM-TG) (i.e., exogenous source) and liver-induced very low density lipoprotein triglycerides (VLDL-TG) (i.e., endogenous source) (Goldberg 2009). The lipids released from the small intestine and the liver are deposited in peripheral sites, such as adipose tissue and skeletal muscle, to be stored as triglycerides or to be utilized as

an energy source. Atherogenic potential is amplified by the remnants of CM, VLDL, and LDL, which are products of lipoprotein lipase-induced VLDL lipolysis (Lusis 2000). These remnants infiltrate the endothelial cells of arteries and lead to the pathogenesis of atherosclerosis (Ginsberg and Fisher 2009). Generally, increased PPTG leads to reduced plasma HDL and increased small, dense LDL, contributing to the pathogenesis of atherosclerosis (Patsch, Esterbauer et al. 2000). There are two sources of triglycerides in the blood: exogenous (CM-TG) and endogenous (VLDL-TG). CM-TG is synthesized in the epithelial cells of the endoplasmic reticulum (ER) and released into the lymphatic system and then circulated through the superior vena cava, while VLDL-TG is produced by the ER of hepatocytes (Goldberg 2009).

Exogenous Pathway Dietary triglycerides are broken down by pancreatic lipase into monoglyerides and free fatty acids and then absorbed through the enterocytes in the small intestine. Free fatty acids and monoglycerides are re-esterified to triglycerides in the ER. Before entering the lymphatic systems, triglycerides are lipidated in apolipoprotein B48, free cholesterol, cholesterol ester and phospholipid to form CMs (Hussain 2000). CM-TG is hydrolyzed by a membrane lipoprotein lipase (mLPL) that is located on the endothelium of blood vessel via heparin sulfate-proteoglycans (Oscai, Essig et al. 1990). mLPL is the main enzyme responsible for TG hydrolysis and also stimulates the uptake of free fatty acids into local tissues. Most free fatty acids are then taken up by adjacent tissues, oxidized and re-esterified into triglycerides (Timlin, Barrows et al. 2005).

Remnants of CM-TG, produced from CM-TG hydrolyzed by mLPL, is delivered to the liver as a primary source for VLDL-TG synthesis (Barrows, Timlin et al. 2005).

Endogenous Pathway On the other hand, VLDL-TG synthesized in the liver with apolipoprotein B100 is circulated in the vessels and hydrolyzed by mLPL activity. The VLDL-TG hydrolyzed by mLPL creates smaller and denser IDL, which is removed by the liver via LDL receptors. Finally, it is broken down into LDL, inducing detrimental effects such as atherosclerosis (Ginsberg, Zhang et al. 2005). However, the relationship between hypertriglyceridemia and atherosclerosis has remained unclear because the development of atherosclerosis is associated with other complex, atherogenic factors such as hypertension, insulin resistance and low HDL concentration as well as the presence of LDL concentration (Williams and Tabas 2005). The development of atherosclerosis is generally initiated by a lesion in the arterial wall, increasing the permeability to macromolecules including LDL and apo B-containing lipoproteins such as remnants of VLDL-TG and CM-TG. Modified macromolecules stimulate proinflamatory responses through lipid oxidation , as a result of reactive oxygen species (ROS). These responses eventually contribute to cell death due to scavenger receptor-mediated uptake of the macromolecules, leading to a necrotic core in the lesion. Plague ruptures and thrombosis occurs, inducing CVD events such as strokes and myocardial infarctions (Ross 1999).

INSULIN ACTION AND POSTPRANDIAL TRIGLYCERIDES

The human body tries to maintain euglycemic homeostasis during resting and exercise. In the postprandial state, beta cells of the pancreas release large amount of insulin for the maintenance of postprandial glucose concentration. Chronic insulin resistance is an initial symptom preceding type 2 diabetes, hyperglycemia and hyperinsulinemia and obesity (Petersen, Dufour et al. 2004; Petersen, Dufour et al. 2007). If it disrupts blood glucose homeostasis, abnormal elevation of plasma glucose concentration occurs (Olefsky and Glass). When skeletal muscle with insulin resistance cannot regulate glucose uptake, the liver is prevented from the insulin-induced suppression of hepatic glucose production and VLDL assembly and secretion. A growing amount of research has shown that the pathogenesis of insulin resistance is significantly correlated with the dysfunction of lipid metabolism in skeletal muscle and the liver (Samuel, Petersen et al. 2010). In addition, low protein expression of the important enzymes required for oxidative phosphorylation, such as pyruvate dehydrogenase, succinate dehydrogenase and cytochrome c oxidase, decreases mitochondrial density in insulin resistant offspring of individuals with type 2 diabetes (Morino, Petersen et al. 2005). Recent studies suggest that the development of insulin resistance is significantly related to decreased mitochondria density and function for fatty acid oxidation (Hulver, Berggren et al. 2003; Toledo, Menshikova et al. 2007). For instance, high fat feeding over 6 months resulted in increased body fat and insulin resistance in a low-aerobic capacity mouse model with low expression of proteins

including skeletal muscle fatty acid oxidation , despite similar energy intake, compared to the high-aerobic capacity group (Noland, Thyfault et al. 2007). This indicates that low fat oxidation with a high-fat diet may accumulate body fat, contributing to exacerbating insulin action.

AEROBIC EXERCISE AND POSTPRANDIAL TRIGLYCERIDES

Even though the beneficial effect of exercise is not fully understood, it is well known that exercise is a primary contributor to improving metabolic disorders such as hypertension and type 2 diabetes (Gill, Al-Mamari et al. 2004; Gill, Al-Mamari et al. 2007). In particular, moderate exercise (approximately 50% VO_{2max}) is effective in decreasing PPTG (Gill, Herd et al. 2002; Burton, Malkova et al. 2008). However, many factors contribute to the magnitude of reduction on PPTG following a single bout of exercise, including exercise intensity, duration, type and energy deficit induced by exercise (Malkova, Evans et al. 2000; Katsanos, Grandjean et al. 2004). Exercise at 50% VO_{2max} over 60 min, for example, reduced PPTG by 9.3%. When exercise duration was extended to 120 min at the same intensity, PPTG was reduced by 22.8% (Gill, Herd et al. 2002). However, the studies related to the change of exercise type, duration and intensity have shown mixed results. While both continuous and intermittent exercises at a given absolute intensity were equally efficient in decreasing PPTG (Miyashita, Burns et al. 2006; Mestek, Plaisance et al. 2008), some studies showed that only intermittent exercise at 60% VO_{2max} (3 × 10 min with 20 min interval between sessions), but not continuous

exercise at 60 % VO_{2max} for 30 min, was effective in reducing PPTG, compared to the sedentary control group (Altena, Michaelson et al. 2004). In addition, Tsetsonis and colleagues showed an equal reduction in PPHG 15 h following completion of either 3 hours of walking at 30% $VO_{2\ max}$ or 90 minutes of energy matched running at 60% $VO_{2\ max}$ (Tsetsonis and Hardman 1996). Conversely, Katsanos and colleagues demonstrated that only moderate intensity exercise at 65% $VO_{2\ max}$ was effective at improving PPGT compared to both energy matched low intensity exercise at 25% $VO_{2\ max}$ and a non-exercise control (Katsanos, Grandjean et al. 2004). These mixed findings are not fully understood; however, the discrepant results may be due to the lack of daily activity and diet controls.

DAILY ACTIVITY AND POSTPRANDIAL TRIGLYCERIDES

Total energy expenditure is composed of basal metabolic rate (RMR), the thermal effect to food intake, daily activity and structure exercise (Levine 2007). Non-exercise daily activity is energy expended through physical activities, such as walking, standing and gardening, except for structured exercise (Levine, Eberhardt et al. 1999). Daily walking contributes to most of the variation in energy expenditure of activity thermogenesis in humans who do not regularly exercise, implying that increased daily activity is adversely associated with increased adiposity (Levine 2007). In addition, daily walking plays a crucial role in reducing obesity and obesity related diseases(Levine, Eberhardt et al. 1999), including insulin resistance, type 2 diabetes, and CVD. Thus, increasing daily

walking is of importance to enhance health (Manson, Greenland et al. 2002; Swartz, Strath et al. 2003) whereas the reduction of daily walking contributes to various health-related metabolic dysfunctions including insulin resistance (Krogh-Madsen, Thyfault et al.). A epidemiological study reported that obesity in Britain were increased by 100% over 2 decades, based on economic development shifting to a more sedentary lifestyle. This shift occurred in spite of decreased energy intake, since decreased energy expenditure could contribute to positive energy balance (Prentice and Jebb 1995). Conversely, the activation of mLPL, particularly in skeletal muscle, was significant to provide resistance to positive energy-induced obesity (Jensen, Schlaepfer et al. 1997). The activation of mLPL, which is a key enzyme to hydrolyze triglyceride-rich lipoprotein, improves insulin sensitivity and triglyceride metabolism(Zderic and Hamilton 2006). Interestingly, slow twitch muscle fibers, mainly activated by ambulatory activity (~50%VO_{2max}) (Bey, Akunuri et al. 2003), maximally stimulated m LPL activity which was not further increased by vigorous intensity exercise (~110%VO_{2max}) (Hamilton, Etienne et al. 1998). However, limited numbers of studies to our knowledge have investigated the effect of daily activity on PPTG levels.

RESEARCH QUESTION

The aim of the present study was to examine the effects of prolonged sitting on PPTG, compared to active walking and standing. In particular, the present study focused on activity control throughout trials and on metabolic variables in PPTG following prolonged sitting or active walking.

Chapter 3

METHODS

SUBJECTS

Seven healthy, active male subjects (age of 25.6 ± 3.7 yr, body mass of 71.4 ± 6.2 kg, and height of 174 ± 5 cm) were participated in a randomized crossover design. Each subject completed all trials. Subjects were allowed to participate only if they were non-smokers and normotensive (<140/90 mm Hg), had a BMI of <30 kg/m^2 with no clinical history of cardio-pulmonary and metabolic diseases and took no medications that could affect lipid or carbohydrate metabolism. All subjects were fully informed of any possible risks and procedures with written informed consent obtained before participation. The study was conducted with an ethical approval from the University of Texas Institutional Review Board.

STUDY DESIGN

Three trials were conducted (Figure 1): 1) Increased walking (~17000 daily steps) with balanced diet (3156 ± 94 kcal) (WB) (high energy expenditure of 3227 ± 73 kcal) - net balance, 2) prolonged sitting (~ 1700 daily steps) with hyper-calories (3156 ±94 kcal) (SH) (low energy expenditure of 2525 ± 77 kcal) - energy surplus and 3) prolonged sitting (~1700 daily steps) with balanced diet (2528 ± 74 kcal) (SB) (low energy

expenditure of 2551± 106 kcal) - net balance. Each subject undertook three intervention trials in a randomized, crossover design, each trial occurring for 5 days with one week interval between trials. Each subject performed all WB, SH and SB trials. Each trial was composed of 3 phases: control (CON) on day 1 (D1) and day 2 (D2), intervention of increased walking or prolonged sitting on day 3 (D3) and day4 (D4), and a high fat tolerance test (HFTT) on day 5 (D5). Throughout all trials, subjects were instructed to refrain from planned exercise. During each 5 day trial, all food was provided from the laboratory. The time point subjects ate each meal was recorded for the first trial and replicated throughout trials. Provided daily food calories were based on the actual daily energy expenditure derived from an activity monitor in preliminary test. On the HFTT day, subjects reported to the laboratory at 0720 following a 13h overnight fast. Body weight and height were measured. A catheter was inserted into forearm, followed by a fasting blood collection.. After subjects consumed the high-fat meal, they sit quietly while working on a computer and watching movies at the end of the HFTT, and blood samples were obtained hourly over 6 hours

ACTIVITY CONTROL

A pedometer (Yamax Digi-Walker SW-200 pedometer; Great Performance Ltd, London, United Kingdom) was worn on the waistline of subjects to monitor the daily step numbers throughout each trial. To monitor body posture and heart rate on D3 and D4, an activity monitor (IDEEA, MiniSun LLC, Fresno, CA) (Zhang, Werner et al. 2003) was

installed to the other side of the subjects' waistline on the evening of D2 until the end of each trial. Subjects were instructed to achieve step numbers ~7500 steps per day which is regarded as a low level of physical activity (Tudor-Locke and Bassett 2004) and steps were evenly distributed throughout the day (~3,000 steps by noon, ~6,000 steps by 5 pm, and ~7,500 steps before bed). On D3 and D4, subjects performed the WB, SH, or SB intervention. For WB, subjects were asked to evenly step ~17,000 steps during the entire day. For SH or SB, subjects were instructed to remain seated throughout much of the day and to maintain the daily step numbers ~ 1700 steps per day. During entire trials, subjects maintained these diet and physical activity requirements by phone and email communication.

HIGH FAT TOLERANCE TEST

Subjects reported to the laboratory at 0720 in the morning on HFTT day following a 13h-overnight fast via automobile transportation and consumed each test meal at the same time of day in a period no longer than 5 min. Five hundred ml of water was provided to subject one hour before the beginning of HFTT. The test meal was prepared, based on body mass at 16.1kcal/kg body mass (1119 ± 135 kcal; 1.2, 1.1 and 0.22 g/kg body weight of fat, carbohydrate and protein, respectively). Any additional fluids consumed during the HFTT were recorded and repeated for the subsequent trials.

BIOCHEMICAL ANALYSIS

All blood samples collected were immediately transferred to K_2 EDTA collection tubes (BD Vacutainer, Franklin Lakes, NJ), centrifuged at 2,000 g for 15 minutes at 4°C. Plasma was then stored in separate aliquots at -80°C until later analysis. All samples for each subject were performed in duplicate within the same run. Plasma triglyceride and glucose were measured by a spectrophotometric method using commercially available kits (Pointe Scientific, Inc. Canton, USA). Plasma insulin was measured with a commercially available human insulin ELISA (Alpco Diagnostics, Salem, USA).

STATISTICAL ANALYSIS

One-way ANOVA with repeated measures was used to compare mean differences in postprandial responses via incremental and the area under the curves(AUC) between trials. Insulin resistance was calculated by using the homeostatic model assessment (HOMA-IR) and the composite whole body insulin sensitivity index, ISI (composite). Fasting plasma TG, glucose, insulin, HOMA-IR, ISI (composite), daily step numbers and body positions across trials were analyzed using one-way ANOVA with repeated measures. For postprandial TG, glucose, and insulin, two-way ANOVA with repeated measures was performed to examine trial and time interaction, followed by post hoc test Fisher's Least Significant Difference (LSD). P-value was set at the 0.05 level for all statistics.

Chapter 4

RESULTS

PHYSICAL ACTIVITY AND ENERGY INTAKE CONTROL

During control days (D1 and D2), there was no difference in step counts across trials (~7500 per day). During the treatment days (D3 and D4), subjects stepped 16900 ± 210, 1631 ± 21 and 1644 ± 20 steps for WB, SH and SB, respectively. Until the end of HFTT on D5, step numbers were not different across trials: 518 ± 25, 456 ± 20, and 453 ± 22 for WB, SH and SB respectively (Figure 2(A)). According to the 24h-body position analysis on D3 and D4 (Figure 2(B)), sitting time was 536 ± 55, 855 ± 41, and 858 ± 59 min for WB, SH, and SB, respectively. Sitting time during SH and SB trial was ~320 min longer than WB trial ($p < 0.001$), showing that WB spent significantly less time sitting than SH and SB (for all, $p < 0.001$). Furthermore, walking time was significantly higher in WB (131 ± 13 min) than both SH (16 ± 1 min) and SB (16 ± 2 min) ($p < 0.001$) with no difference between SH and SB (Figure 2(B)). During intervention period (D3 and D4), time spent standing in WB, SH, and SB (308 ± 66, 97 ± 45 and 111 ± 51 min, respectively). Furthermore, sleeping time was not different across trials (449 ± 39, 457 ± 32, and 441 ± 40 min) (Figure 2(B)).

PLASMA CONCENTRATIONS

In the fasted state, plasma triglycerides were significantly lower in WB by 23% compared to SH ($p < 0.05$) while glucose, and insulin concentrations were not significantly different across trials (Figure 4). In the postprandial state, WB reduced AUC_T TG by 21.3% compared to SH ($p < 0.001$) and by 19.7% compared to SB (N.S.; $p = 0.055$). WB reduced the AUC_I TG, compared to SH by 17.4% ($p < 0.005$) and SB by 20.1% ($p < 0.05$), respectively (Figure 4). The AUC_I of plasma glucose was lower in WB than SH by 50.5% ($p < 0.005$) and SB by 49.5% (NS, $p = 0.057$) (Figure 5). Both AUC_T and AUC_I *of* plasma insulin were lower in WB, compared to SH by 19.4% and 18.8 ($p < 0.005$) and 0.05), respectively (Figure 6).

Chapter 5

DISCUSSION

The metabolic response to prolonged sitting with hyper or balanced caloric intake was measured for 2 days. The key findings of the present study are that prolonged sitting with hyper or balanced energy intake, compared to walking with balanced energy intake, significantly increased the concentration of postprandial plasma triglycerides and reduced whole body insulin action. Prolonged sitting trials, independent of energy intake, equally impaired plasma triglycerides, indicating that prolonged sitting has primarily negative effects on PPTG. No differences were shown in plasma triglycerides concentration between SB and SH despite the diet modifications. These findings indicate that not only is daily activity important for enhancing postprandial metabolism, but also that prolonged sitting has detrimental consequences on metabolic responses in the concentration of plasma triglycerides, independent of energy intake.

It is well known that increased daily walking improves insulin resistance in humans, while prolonged sitting leads to a rapid decrease in insulin action (Stephens, Granados et al.; Miyatake, Nishikawa et al. 2002). In addition, recent epidemiological studies reported that prolonged sitting increases the risk of metabolic disorders such as obesity and type 2 diabetes (Fung, Hu et al. 2000; Hu, Leitzmann et al. 2001). In particular, reduced non-exercise activity contributes to potential detrimental results on metabolic reactions, including insulin resistance (Seider, Nicholson et al. 1982; Hamilton, Hamilton et al.

2004). In agreement with the present study, previous studies reported that the reduction of insulin action was observed following short terms of inactivity intervention in both humans and rats (Lipman, Raskin et al. 1972; Ploug, Ohkuwa et al. 1995). Moreover, in the postprandial state, a sedentary lifestyle may exacerbate postprandial metabolic responses (Nordestgaard, Benn et al. 2007). Ginsberg and colleagues (Ginsberg, Zhang et al. 2005) demonstrated that a hyper caloric diet changes energy partitioning, leading to liver insensitivity to insulin action. This prevents the liver from suppressing VLDL assembly and secretion. The findings of the present study show that insulin action was significantly reduced following a short period of prolonged sitting, i.e., 2 days, concurrent with an energy surplus (~ 19.4%, $p< 0.005$), indicating that inactivity with a hyper caloric diet may contribute to more detrimental consequences for insulin action. Therefore, results of the present study suggest that a hyper caloric diet, in addition to prolonged sitting, plays a crucial role in exacerbating acute insulin reactions.

The result of the present study is quite different from the findings of Stephens et al (Stephens, Granados et al.) which demonstrated that prolonged sitting, while maintaining an energy surplus for a day, significantly increased the detrimental effects on insulin action, compared to prolonged sitting with a balanced caloric diet ($p= 0.04$). The discrepancy of the findings might result from differences in net energy balance, standing time, and daily step counts between Stephens et al and the present study (roughly 1000 kcal *v*s 600 kcal, 20 min *v*s 120 min and 264 steps *v*s 1650 steps per day, respectively). This implies that different amount of energy intake and daily activity during prolonged sitting may contribute to the discrepant results. In addition, during prolonged sitting,

there were significantly higher step counts per day in the present study, compared to Stephens findings. This may maintain the activation of slow twitch muscle fibers over a certain level since slow twitch muscle fibers, mainly activated by ambulatory activity, stimulated m LPL activity in skeletal muscle (Bey, Akunuri et al. 2003). Recent studies reported that following 7 days of bed rest, peripheral and whole-body insulin action were significantly reduced, even though hepatic insulin sensitivity was not impaired (Mikines, Richter et al. 1991; Blanc, Normand et al. 2000). This indicates that skeletal muscle, specifically mLPL activity, is a primary candidate for the detrimental effects of inactivity. Taken together, reduced muscle activity such as decreased mLPL activity, following inactivity plays an important role in lowering metabolic responses.

From this perspective, the magnitude of the reduced plasma triglyceride concentration in WB is robust following 2 days of walking, compared to both SH and SB since increased walking in an acute period of time may increase mLPL activity in skeletal muscle. This provides an early positive metabolic response to reduce the concentration of plasma triglycerides on PPTG, compared to prolonged sitting, independent of energy intake. Potential mechanisms for explaining the effects of walking and sitting on PPTG could be related to energy redistribution as well as mLPL activity. Walking and standing for 2 days may contribute to the depletion of hepatic glycogen and triglycerides, causing the liver to redistribute energy. When the liver redistributes energy, it induces suppression in VLDL production and secretion into the circulation on PPTG. Partitioning of substrates, such as remnants of CM and glucose, to the liver is a main factor in determining the production and secretion of VLDL-TG (Timlin, Barrows et al. 2005). It is well

established that the day following a bout of exercise 3-hydroxybutyrate, an index of hepatic triglyceride oxidation, increases in PPTG (Burton, Malkova et al. 2008; Harrison, O'Gorman et al. 2009). From this perspective, active walking increases hepatic glycogen and triglyceride usage, leading to energy depletion in the liver. Depleted energy in the liver may increase hepatic triglyceride oxidation and energy utilization in which VLDL production and secretion is reduced, also decreasing plasma TG concentration. However, complex mechanisms are likely responsible for increased insulin action and reduced plasma triglycerides in response to active walking. Taken together, increased walking may induce the depletion of triglycerides and glycogen in the liver and may change energy partitioning and utilization in favorable ways in order to reduce the detrimental effects on PPTG.

A second explanation is that the stimulation of mLPL activity, as a result of active walking, may be a primary factor in the improved clearance in PPTG because mLPL is the rate limiting enzyme for triglyceride lipolysis on the luminal surface of capillary endothelial cells (Oscai, Essig et al. 1990). Kiens et al reported that mLPL activity is stimulated in humans even after short-term exercise training (Kiens, Lithell et al. 1989). However, this activation is decreased by detraining (Simsolo, Ong et al. 1993) and physical inactivity (Hamilton, Hamilton et al. 2004). In this respect, the activation of mLPL, to the extent of the present findings, may stimulate walking-modified attenuation of PPTG. Therefore, prolonged sitting trials in the present study may reduce mLPL activity, which may in turn increase plasma triglyceride concentration by 20% compared to walking trial in PPTG. However, Katsanos et al suggested it is unclear whether

improved mLPL activity contributes to an walking-induced reduction of PPTG based on a finding showing no strong correlation between enhanced mLPL activity and reduction in PPTG (Katsanos and Moffatt 2004). More carefully controlled and well-designed studies are required in order to improve current understanding of the correlation between daily activity, energy intake and metabolic responses.

In conclusion, the findings of the present study show that prolonged sitting for 2 days can decrease insulin action and increase plasma triglyceride concentration in the postprandial state. Prolonged sitting with or without a change in energy intake causes the detrimental effects on metabolic responses. This implies that other factors besides energy surplus may be involved in the process. The results in our study provide evidence for a strong relationship between time spent, increased walking and enhanced metabolic health as proposed in the tenets describing the inactivity physiology paradigm (Hamilton, Hamilton et al. 2007), indicating the importance of maintaining at least daily low-intensity activity to minimize the harmful effects of physical inactivity on metabolic health.

Limitations and Control for Confounding Variables

The use of young, healthy, non-obese subjects may limit the generalizability of the study results to other populations. We chose to study the metabolic responses to prolonged sitting in recreationally active, but not highly trained individuals to minimize potential confounding effects of disease processes, reported in overweight individuals with low

physical activity. Future studies are required to determine if factors such as aging, obesity, or chronically low levels of physical activity impact the response to inactivity.

FIGURE LEGEND

Figure 1: Experimental protocol

Figure 2: Daily steps (A) and mean distribution of body position (D3-D4) (B) during WB, SH and SB trials. *Significantly higher in WB than SH and SB ($p<0.005$); #Significantly lower in WB than SH and SB ($p<0.005$). Values are expressed as mean ± SD.

Figure 3: Daily energy expenditure (A), consumption (B) and net energy balance (C) during WB, SH and SB. Intervention periods (D3-D4). *Significantly different from WB; #Significantly different from SB; **Significantly different from SH (for all, $p<0.001$).

Figure 4: Fasting and postprandial plasma triglycerides concentrations before and after HFTT over 6 hr (A) and the total and incremental area under the curves (AUC) of plasma triglycerides during HFTT (B). Values for AUCs are % of SH. *Significantly different from WB ($p<0.05$); **from WB ($p<0.005$).

Figure 5: Plasma glucose concentrations during HFTT over 6 hr. *Significantly different from WB ($p<0.05$).

Figure 6: Plasma insulin concentrations on HFTT over 6 hr (A). and total and incremental AUC of plasma insulin during HFTT (B). Values for AUCs are % of SH. *Significantly different from WB ($p<0.05$); **from WB ($p<0.005$).

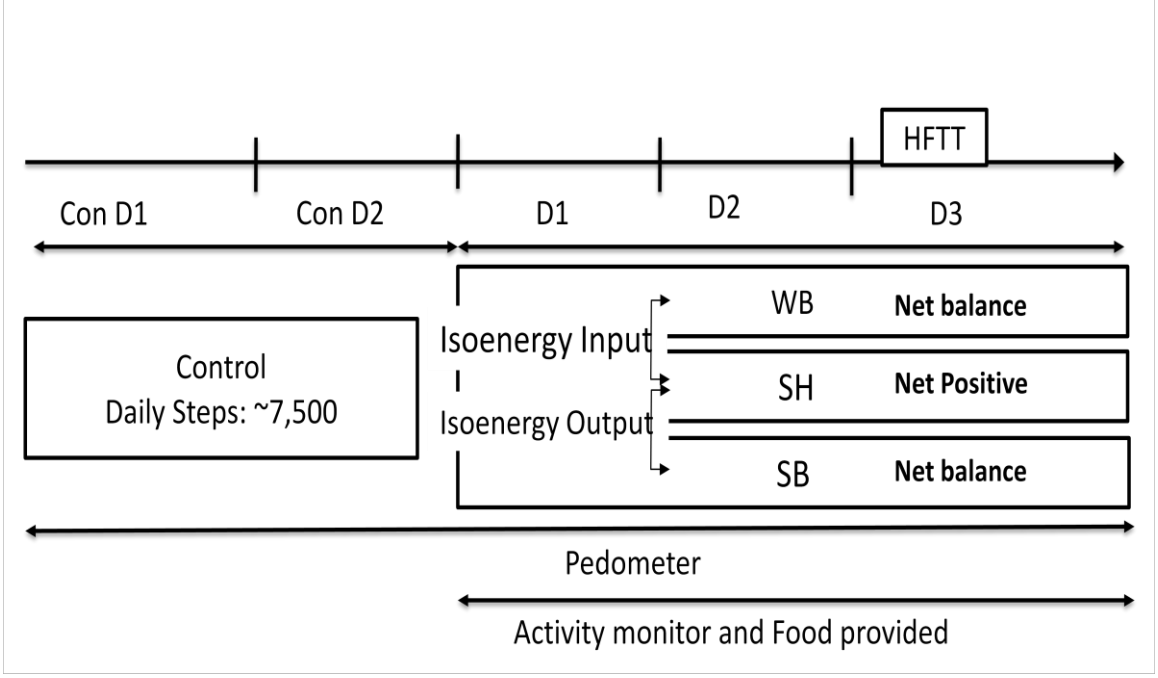

Figure 1: Experimental protocol

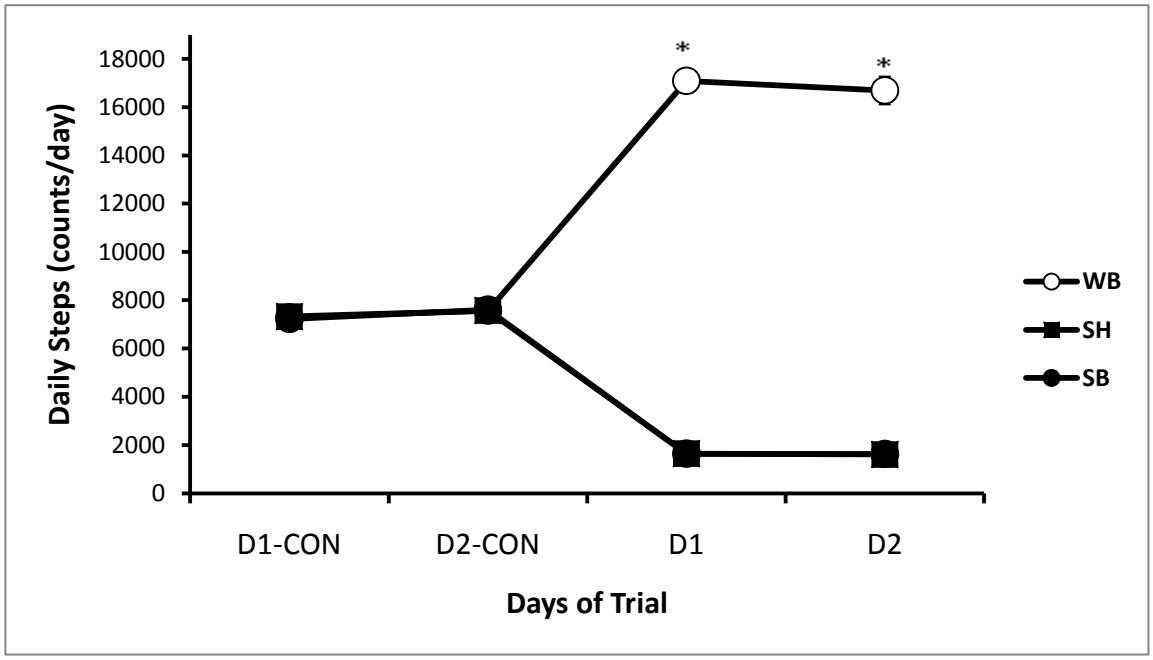

Figure 2(A): Daily steps (D1-D4) during WB, SH and SB trials. *Significantly higher in WB than SH and SB ($p<0.005$). Values are expressed as mean ± SD.

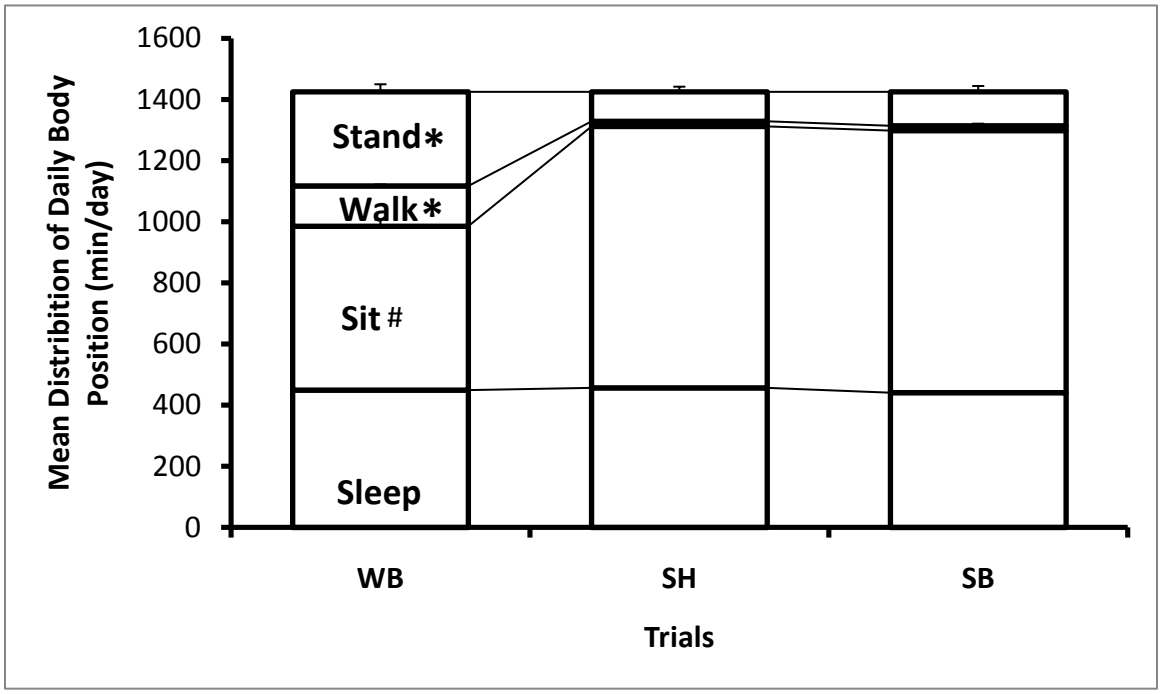

Figure 2(B): Mean distribution of body position (D3-D4) during WB, SH and SB trials. *Significantly higher in WB than SH and SB ($p<0.005$); #Significantly lower in WB than SH and SB ($p<0.005$). Values are expressed as mean ± SD.

Figure 3(A): Daily energy expenditure during WB, SH and SB. Intervention periods (D3-D4). *Significantly higher in WB ($p<0.05$).

Figure 3(B): Daily energy consumption during WB, SH and SB. Intervention periods (D3-D4). #Significantly lower in WB and SB ($p < 0.001$).

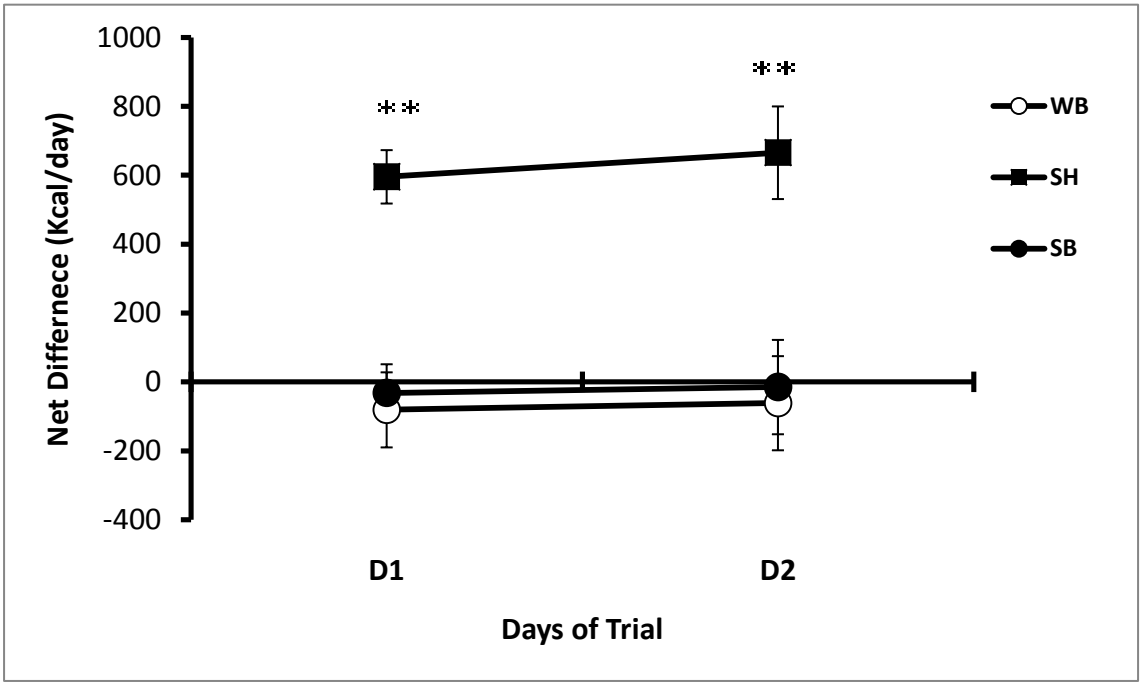

Figure 3(C): Daily net energy balance during WB, SH and SB. Intervention periods (D3-D4). **Significantly higher in SH ($p < 0.001$).

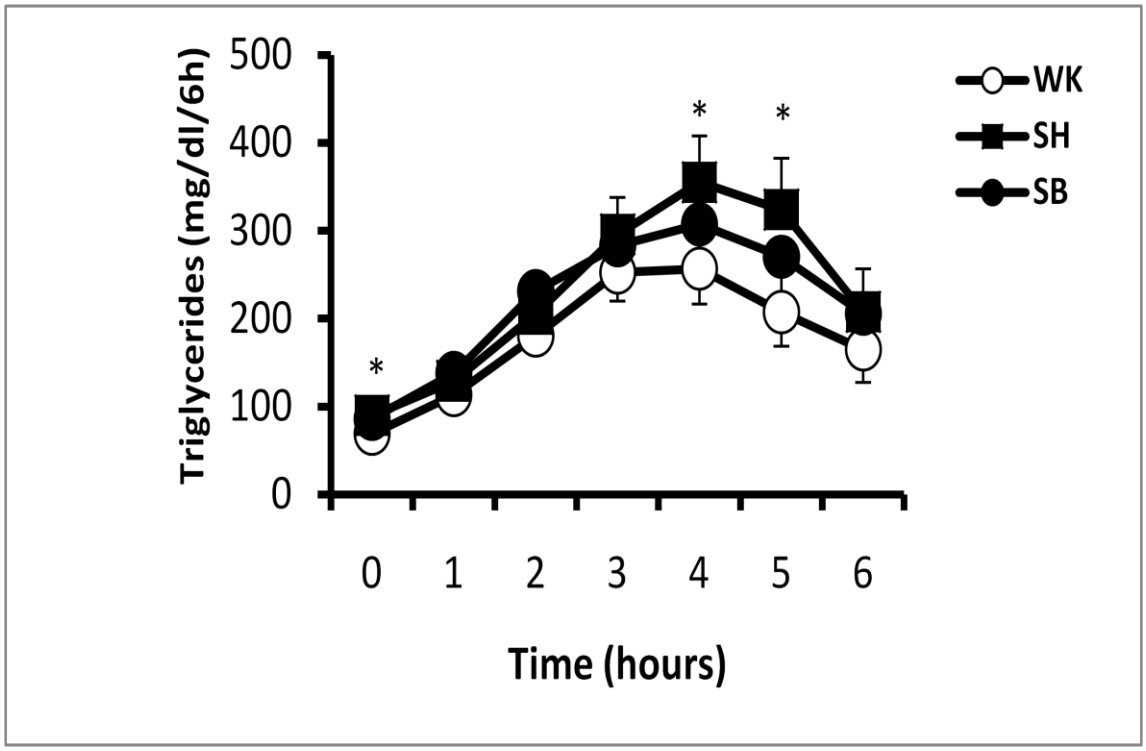

Figure 4(A): Fasting and postprandial plasma triglycerides concentrations before and after HFTT over 6 hr. Values for AUCs are % of SH. *Significantly different from WB ($p<0.05$).

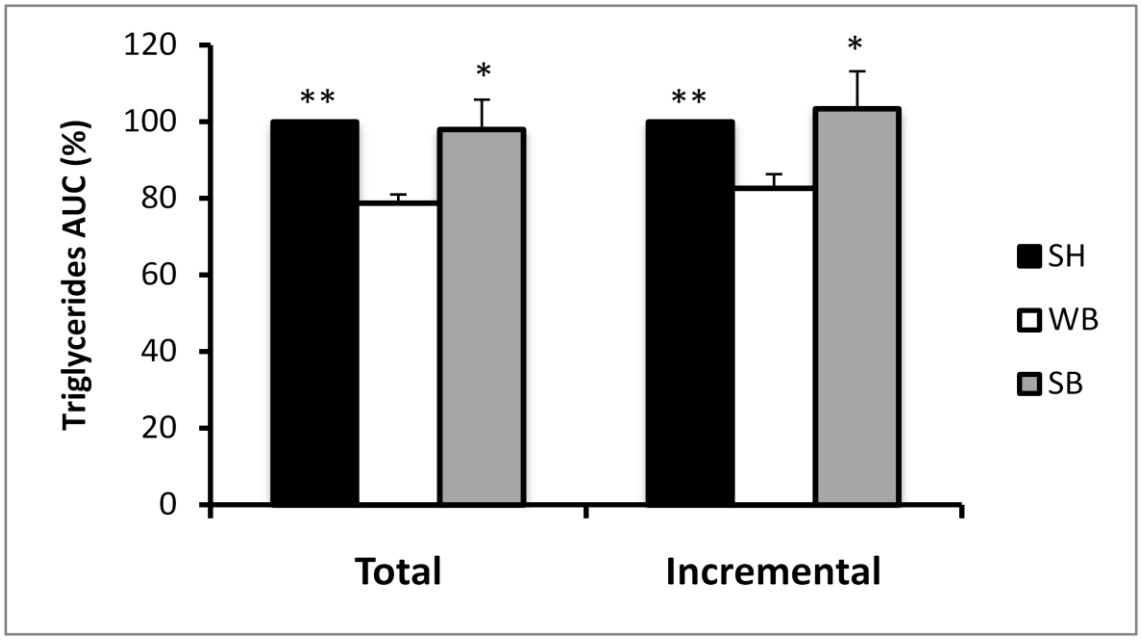

Figure 4(B): The total and incremental area under the curves (AUC) of plasma triglycerides during HFTT. Values for AUCs are % of SH. *Significantly different from WB ($p<0.05$) and **significantly different from WB ($p<0.005$).

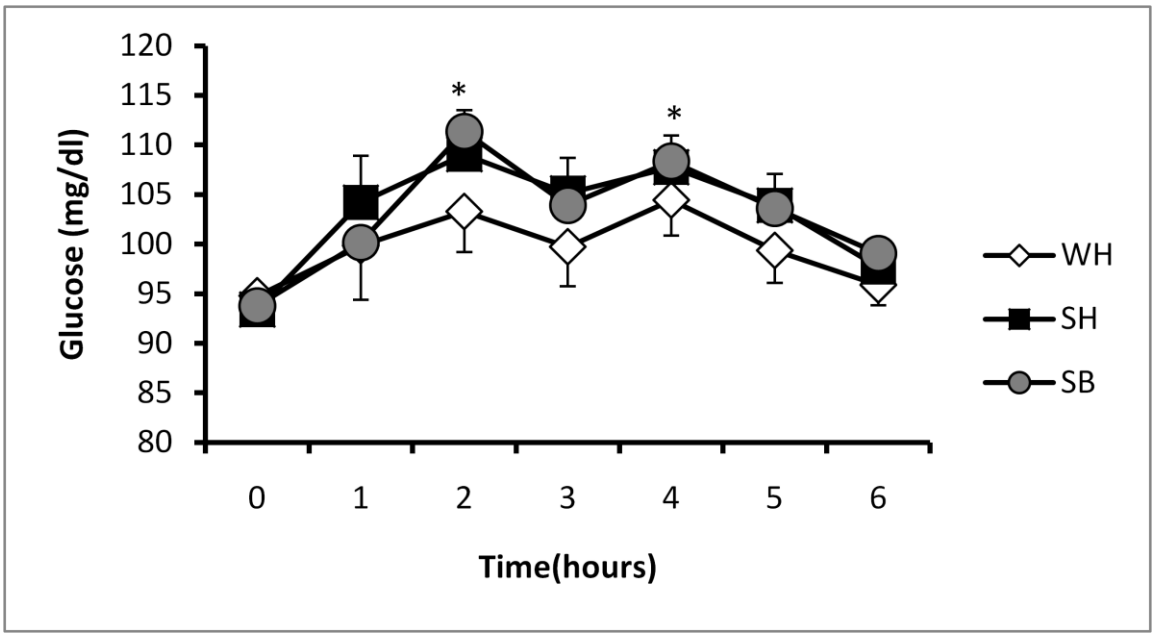

Figure 5: Plasma glucose concentrations during HFTT over 6 hr. *Significantly different from WB ($p<0.05$).

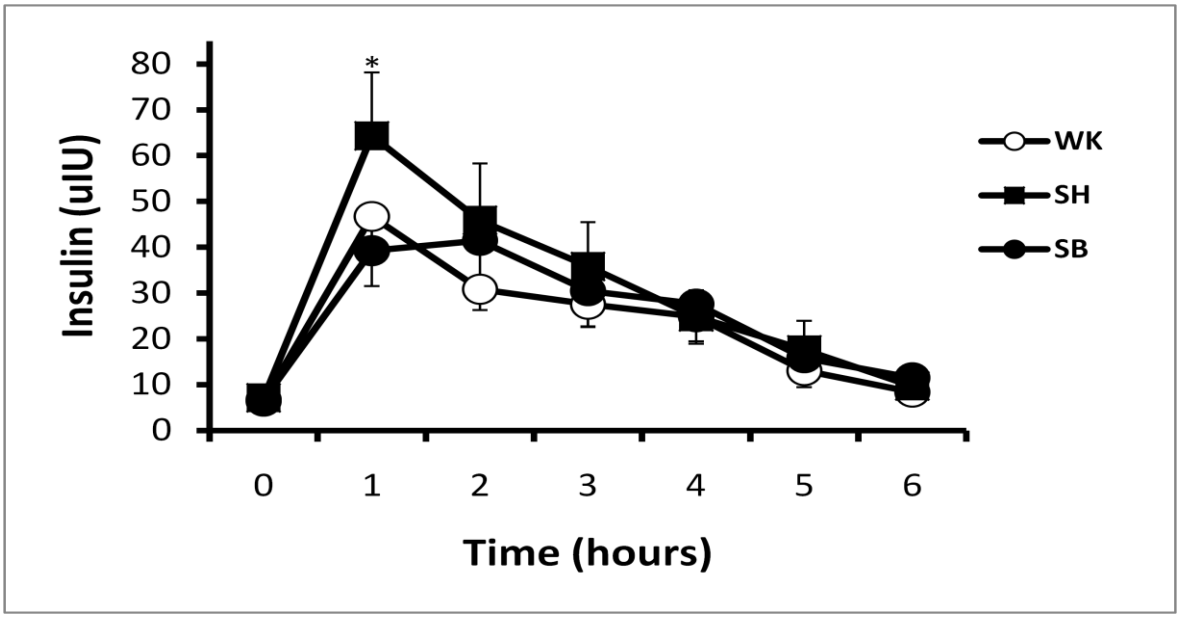

Figure 6(A): Plasma insulin concentrations on HFTT over 6 hr. *Significantly different from WB ($p<0.05$).

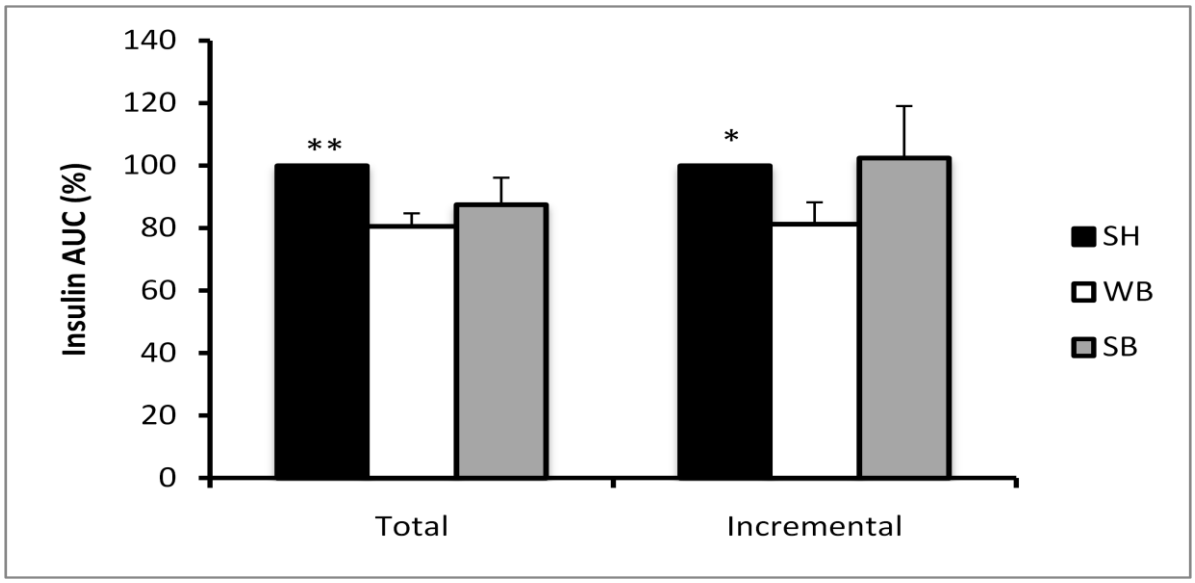

Figure 6(B): Total and incremental AUC of plasma insulin during HFTT. Values for AUCs are % of SH. *Significantly different from WB ($p<0.05$). **from WB ($p<0.005$).

APPENDIX

MEASUREMENTS OF PLASMA CONCENTRATIONS

Plasma Triglycerides Measurement

Plasma triglyceride is measured by a spectrophotometric method using commercially available kits (Pointe Scientific, Inc. Canton, USA). The plasma samples are removed from freezer (-80°C) and thawed in an ice-water bath. 5ul of plasma sample will be added to 300ul of triglyceride reagent. Triglycerides in the sample are hydrolyzed by lipase to glycerol and fatty acids. The glycerol is then phosphorylated by ATP to glycerol 3-phosphate (G-3-P) and ADP in a reaction catalyzed by glycerol kinase (GK). G-3-P is then converted to dihydroxyacetone phosphate (DHAP) and hydrogen peroxide in a reaction catalyzed by glycerophosphate oxidase (GPO). The hydrogen peroxide then reacts with 4-aminoantipyrine and 3-hydroxy-2,4,6-tribomobenzoic (TBHB)in a reaction catalyzed by peroxidase to form a red colored quinoneimine dye. The absorbance of the red colored quinoneimine dye is measured spectrophotometrically at 340 nm. The intensity of the color produced is directly proportional to the concentration of triglycerides in the sample.

Reactions:

1. TG --- *Lipase* ---> Glycerol + Fatty Acids
2. Glycerol + ATP --- *GK*---> G-3-P + ADP
3. G-3-P + O2 --- *GPO*---> DHAP + H_2O_2
4. H_2O_2 + TBHB --- *Peroxidase*--- > Ouinoneimine dye + $2H_2O$

Plasma Glucose Measurement:

Plasma glucose is measured by a spectrophotometric method using commercially available kits (Pointe Scientific, Inc. Canton, USA). The plasma samples are removed from freezer (-80°C) and thawed in an ice-water bath. 5 uL of plasma sample is added to 1,000 uL of glucose reagent and then incubated at room temperature for 3 minutes. Glucose is phosphorylated with ATP to produce glucose 6-phosphate (G-6-P) in the reaction catalyzed by hexokinae (HK). The glucose 6-phosphate is then oxidized with concomitant reduction of NAD to NADH in the reaction catalyzed by glucose 6-phosphate dehydrogenase (G6PDH). The absorbance of NADH formed will be measured at 340 nm. The concentration of NADH is directly proportional to the concentration of glucose in the sample.

Hexokinae Reaction:

Reaction 1: Glucose + ATP ---- *HK* ---> G-6-P + ADP

Reaction 2: G-6-P + NAD ---- G6PDH ---> 6-Phosphogluconate + NADH + H^+

Plasma Insulin Measurement:

The concentration of plasma insulin is determined with a commercially available human insulin enzyme-linked immunosorbent assay (Alpco Diagnostics, Salem, USA). The assay is a sandwich type immunoassay. The 96 well microplate is coated with a monoclonal antibody specific to insulin. The plasma samples are removed from freezer (-80°C) and thawed in an ice-water bath. 25 uL of plasma sample is transferred to the microplate wells. Insulin binds monoclonal insulin primary antibody coated on the well. 100 uL of enzyme conjugate will be then added to the wells. The microplate is then incubated on an orbital imcroplate shaker at 750 rpm for 60 minutes. Enzyme-linked secondary antibody (horseradish peroxidase-antibody) binds the monoclonal insulin primary antibody.

After 1st incubation, the wells are then washed with wash buffer and blotted dry. Substrate is added and then incubated on an orbital microplate shaker at 750 rpm for 15 minutes. The substrate reacts with horseradish peroxidase to produce colored products. After 2nd incubation, stop solution is added to stop the reaction. The absorbance of insulin is measured spectrometrically at 450 nm with reference wavelength of 620 nm. The intensity of the color generated is directly proportional to the concentration of insulin in the sample.

REFERENCE

Altena, T. S., J. L. Michaelson, et al. (2004). "Single sessions of intermittent and continuous exercise and postprandial lipemia." Med Sci Sports Exerc **36**(8): 1364-71.

Barrows, B. R., M. T. Timlin, et al. (2005). "Spillover of dietary fatty acids and use of serum nonesterified fatty acids for the synthesis of VLDL-triacylglycerol under two different feeding regimens." Diabetes **54**(9): 2668-73.

Bey, L., N. Akunuri, et al. (2003). "Patterns of global gene expression in rat skeletal muscle during unloading and low-intensity ambulatory activity." Physiol Genomics **13**(2): 157-67.

Blanc, S., S. Normand, et al. (2000). "Fuel homeostasis during physical inactivity induced by bed rest." J Clin Endocrinol Metab **85**(6): 2223-33.

Boquist, S., G. Ruotolo, et al. (1999). "Alimentary lipemia, postprandial triglyceride-rich lipoproteins, and common carotid intima-media thickness in healthy, middle-aged men." Circulation **100**(7): 723-8.

Burton, F. L., D. Malkova, et al. (2008). "Energy replacement attenuates the effects of prior moderate exercise on postprandial metabolism in overweight/obese men." Int J Obes (Lond) **32**(3): 481-9.

Chakravarthy, M. V. and F. W. Booth (2004). "Eating, exercise, and "thrifty" genotypes: connecting the dots toward an evolutionary understanding of modern chronic diseases." J Appl Physiol **96**(1): 3-10.

Fung, T. T., F. B. Hu, et al. (2000). "Leisure-time physical activity, television watching, and plasma biomarkers of obesity and cardiovascular disease risk." Am J Epidemiol **152**(12): 1171-8.

Gill, J. M., A. Al-Mamari, et al. (2007). "Effect of prior moderate exercise on postprandial metabolism in men with type 2 diabetes: heterogeneity of responses." Atherosclerosis **194**(1): 134-43.

Gill, J. M., S. L. Herd, et al. (2002). "Moderate exercise and post-prandial metabolism: issues of dose-response." J Sports Sci **20**(12): 961-7.

Gill, J. M. R., A. Al-Mamari, et al. (2004). "Effects of prior moderate exercise on postprandial metabolism and vascular function in lean and centrally obese men." J. Am. Coll. Cardiol. **44**(12): 2375-2382.

Ginsberg, H. N. and E. A. Fisher (2009). "The ever-expanding role of degradation in the regulation of apolipoprotein B metabolism." J Lipid Res **50 Suppl**: S162-6.

Ginsberg, H. N., Y. L. Zhang, et al. (2005). "Regulation of plasma triglycerides in insulin resistance and diabetes." Arch Med Res **36**(3): 232-40.

Goldberg, I. J. (2009). "Hypertriglyceridemia: impact and treatment." Endocrinol Metab Clin North Am **38**(1): 137-49.

Hamilton, M. T., J. Etienne, et al. (1998). "Role of local contractile activity and muscle fiber type on LPL regulation during exercise." Am J Physiol **275**(6 Pt 1): E1016-22.

Hamilton, M. T., D. G. Hamilton, et al. (2004). "Exercise physiology versus inactivity physiology: an essential concept for understanding lipoprotein lipase regulation." Exerc Sport Sci Rev **32**(4): 161-6.

Hamilton, M. T., D. G. Hamilton, et al. (2007). "Role of low energy expenditure and sitting in obesity, metabolic syndrome, type 2 diabetes, and cardiovascular disease." Diabetes **56**(11): 2655-67.

Harrison, M., D. J. O'Gorman, et al. (2009). "Influence of acute exercise with and without carbohydrate replacement on postprandial lipid metabolism." J Appl Physiol **106**(3): 943-9.

Hu, F. B. (2003). "Sedentary lifestyle and risk of obesity and type 2 diabetes." Lipids **38**(2): 103-8.

Hu, F. B., M. F. Leitzmann, et al. (2001). "Physical activity and television watching in relation to risk for type 2 diabetes mellitus in men." Arch Intern Med **161**(12): 1542-8.

Hulver, M. W., J. R. Berggren, et al. (2003). "Skeletal muscle lipid metabolism with obesity." Am J Physiol Endocrinol Metab **284**(4): E741-7.

Hussain, M. M. (2000). "A proposed model for the assembly of chylomicrons." Atherosclerosis **148**(1): 1-15.

Jensen, D. R., I. R. Schlaepfer, et al. (1997). "Prevention of diet-induced obesity in transgenic mice overexpressing skeletal muscle lipoprotein lipase." Am J Physiol Regulatory Integrative Comp Physiol **273**(2): R683-689.

Katsanos, C. S., P. W. Grandjean, et al. (2004). "Effects of low and moderate exercise intensity on postprandial lipemia and postheparin plasma lipoprotein lipase activity in physically active men." J Appl Physiol **96**(1): 181-188.

Katsanos, C. S. and R. J. Moffatt (2004). "Acute effects of premeal versus postmeal exercise on postprandial hypertriglyceridemia." Clin J Sport Med **14**(1): 33-9.

Kiens, B., H. Lithell, et al. (1989). "Effects of insulin and exercise on muscle lipoprotein lipase activity in man and its relation to insulin action." J Clin Invest **84**(4): 1124-9.

Kolovou, G. D., K. K. Anagnostopoulou, et al. (2005). "Postprandial lipemia in men with metabolic syndrome, hypertensives and healthy subjects." Lipids Health Dis **4**: 21.

Krogh-Madsen, R., J. P. Thyfault, et al. "A 2-wk reduction of ambulatory activity attenuates peripheral insulin sensitivity." J Appl Physiol **108**(5): 1034-40.

Levine, J. A. (2007). "Nonexercise activity thermogenesis--liberating the life-force." J Intern Med **262**(3): 273-87.

Levine, J. A., N. L. Eberhardt, et al. (1999). "Role of nonexercise activity thermogenesis in resistance to fat gain in humans." Science **283**(5399): 212-4.

Levine, J. A., M. W. Vander Weg, et al. (2006). "Non-exercise activity thermogenesis: the crouching tiger hidden dragon of societal weight gain." Arterioscler Thromb Vasc Biol **26**(4): 729-36.

Lipman, R. L., P. Raskin, et al. (1972). "Glucose intolerance during decreased physical activity in man." Diabetes **21**(2): 101-7.

Lusis, A. J. (2000). "Atherosclerosis." Nature **407**(6801): 233-41.

Malkova, D., R. D. Evans, et al. (2000). "Prior exercise and postprandial substrate extraction across the human leg." Am J Physiol Endocrinol Metab **279**(5): E1020-8.

Manson, J. E., P. Greenland, et al. (2002). "Walking compared with vigorous exercise for the prevention of cardiovascular events in women." N Engl J Med **347**(10): 716-25.

Mestek, M. L., E. P. Plaisance, et al. (2008). "Aerobic exercise and postprandial lipemia in men with the metabolic syndrome." Med Sci Sports Exerc **40**(12): 2105-11.

Mikines, K. J., E. A. Richter, et al. (1991). "Seven days of bed rest decrease insulin action on glucose uptake in leg and whole body." J Appl Physiol **70**(3): 1245-54.

Miyashita, M., S. F. Burns, et al. (2006). "Exercise and postprandial lipemia: effect of continuous compared with intermittent activity patterns." Am J Clin Nutr **83**(1): 24-9.

Miyashita, M., S. F. Burns, et al. (2008). "Accumulating short bouts of brisk walking reduces postprandial plasma triacylglycerol concentrations and resting blood pressure in healthy young men." Am J Clin Nutr **88**(5): 1225-31.

Miyatake, N., H. Nishikawa, et al. (2002). "Daily walking reduces visceral adipose tissue areas and improves insulin resistance in Japanese obese subjects." Diabetes Res Clin Pract **58**(2): 101-7.

Morino, K., K. Petersen, et al. (2005). "Reduced mitochondrial density and increased IRS-1 serine phosphorylation in muscle of insulin-resistant offspring of type 2 diabetic parents." J Clin Invest **115**(12): 3587-93.

Noland, R. C., J. P. Thyfault, et al. (2007). "Artificial selection for high-capacity endurance running is protective against high-fat diet-induced insulin resistance." Am J Physiol Endocrinol Metab **293**(1): E31-41.

Nordestgaard, B. G., M. Benn, et al. (2007). "[Non-fasting triglycerides and risk of for myocardial infarction and death among women and men]." Ugeskr Laeger **169**(45): 3865-8.

Nordestgaard, B. G., M. Benn, et al. (2007). "Nonfasting triglycerides and risk of myocardial infarction, ischemic heart disease, and death in men and women." JAMA **298**(3): 299-308.

Olefsky, J. M. and C. K. Glass "Macrophages, inflammation, and insulin resistance." Annu Rev Physiol **72**: 219-46.

Oscai, L. B., D. A. Essig, et al. (1990). "Lipase regulation of muscle triglyceride hydrolysis." J Appl Physiol **69**(5): 1571-7.

Patsch, W., H. Esterbauer, et al. (2000). "Postprandial lipemia and coronary risk." Curr Atheroscler Rep **2**(3): 232-42.

Petersen, K. F., S. Dufour, et al. (2004). "Impaired Mitochondrial Activity in the Insulin-Resistant Offspring of Patients with Type 2 Diabetes." N. Engl. J. Med. **350**(7): 664-671.

Petersen, K. F., S. Dufour, et al. (2007). "The role of skeletal muscle insulin resistance in the pathogenesis of the metabolic syndrome." Proc Natl Acad Sci U S A **104**(31): 12587-94.

Ploug, T., T. Ohkuwa, et al. (1995). "Effect of immobilization on glucose transport and glucose transporter expression in rat skeletal muscle." Am J Physiol **268**(5 Pt 1): E980-6.

Prentice, A. M. and S. A. Jebb (1995). "Obesity in Britain: gluttony or sloth?" BMJ **311**(7002): 437-9.

Ross, R. (1999). "Atherosclerosis is an inflammatory disease." Am Heart J **138**(5 Pt 2): S419-20.

Samuel, V., K. Petersen, et al. (2010). "Lipid-induced insulin resistance: unravelling the mechanism." Lancet **375**(9733): 2267-77.

Seider, M. J., W. F. Nicholson, et al. (1982). "Insulin resistance for glucose metabolism in disused soleus muscle of mice." Am J Physiol **242**(1): E12-8.

Simsolo, R. B., J. M. Ong, et al. (1993). "The regulation of adipose tissue and muscle lipoprotein lipase in runners by detraining." J Clin Invest **92**(5): 2124-30.

Smyth, S. and A. Heron (2006). "Diabetes and obesity: the twin epidemics." Nat Med **12**(1): 75-80.

Stephens, B. R., K. Granados, et al. "Effects of 1 day of inactivity on insulin action in healthy men and women: interaction with energy intake." Metabolism.

Swartz, A. M., S. J. Strath, et al. (2003). "Increasing daily walking improves glucose tolerance in overweight women." Prev Med **37**(4): 356-62.

Timlin, M. T., B. R. Barrows, et al. (2005). "Increased dietary substrate delivery alters hepatic fatty acid recycling in healthy men." Diabetes **54**(9): 2694-701.

Toledo, F. G., E. V. Menshikova, et al. (2007). "Effects of physical activity and weight loss on skeletal muscle mitochondria and relationship with glucose control in type 2 diabetes." Diabetes **56**(8): 2142-7.

Tsetsonis, N. V. and A. E. Hardman (1996). "Reduction in postprandial lipemia after walking: influence of exercise intensity." Med Sci Sports Exerc **28**(10): 1235-42.

Tudor-Locke, C. and D. R. Bassett, Jr. (2004). "How many steps/day are enough? Preliminary pedometer indices for public health." Sports Med **34**(1): 1-8.

Williams, K. J. and I. Tabas (2005). "Lipoprotein retention--and clues for atheroma regression." Arterioscler Thromb Vasc Biol **25**(8): 1536-40.

Zderic, T. W. and M. T. Hamilton (2006). "Physical inactivity amplifies the sensitivity of skeletal muscle to the lipid-induced downregulation of lipoprotein lipase activity." J Appl Physiol **100**(1): 249-57.

Zhang, K., P. Werner, et al. (2003). "Measurement of human daily physical activity." Obes Res **11**(1): 33-40.

Zilversmit, D. B. (1979). "Atherogenesis: a postprandial phenomenon." Circulation **60**(3): 473-85.

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